REMARKS

In the Office Action mailed May 29, 2001, Claims 61 and 87 have been objected to due to informalities. Claim 61 has been cancelled without prejudice. Claim 87 has been amended to correct a typographical error.

Claim 87 has been further objected to as a substantial duplicate of Claim 86. Claim 87 has been amended to replace SEQ ID NO: 20 by SEQ ID NO:18, and Claim 84 has been amended to delete the second sentence, thus correcting inadvertent typographical errors. In view of the foregoing amendments, withdrawal of the objection to Claims 61 and 87 is respectfully requested.

Claims 45-60 and 64-75 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 1-20 of U.S. Patent No. 5,929,040. Claims 61-63 and 76-87 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over Claims 30-36 of co-pending application Serial No. 09/199,926. Upon indication of allowable subject matter in the present application Applicants will, if appropriate, file terminal disclaimers.

Claims 45-87 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner has alleged that the recitation "chemical analogue" in Claims 45-60 and 64-87 is indefinite. Applicants submit that the term is clear and definite to one of ordinary skill in the art. The specification defines the term "chemical analogue" at page 25, lines 13-24, as a nucleic acid having a modified base, nucleotide, nucleoside, or phosphate backbone.

It is clear from the referenced passage that the term does not extend to a change in the number or sequence of bases. Accordingly, the term is clear and definite to one of ordinary skill in the art.

Claim 45 is allegedly indefinite in the recitation "and/or other medical disorders." In the interest of advancing prosecution, the recitation has been deleted from Claim 45.

Claims 61-63 are allegedly indefinite for a variety of reasons set forth in the Office Action at pages 5 and 6. In the interest of advancing prosecution, Claims 61-63 have been cancelled without prejudice. Applicants reserve the right to file a continuation application directed to the subject matter of Claims 61-63.

Claims 64-75 are allegedly indefinite in the recitation "directed from." In accordance with the Examiner's suggestion, the word "directed" has been replaced by "transcribed" in Claim 64.

Claim 76 allegedly lacks antecedent basis for the term "the mammal." Claim 76 has been amended to provide proper antecedent basis.

Claim 84 is allegedly indefinite because it contains two sentences. Claim 84 has been amended to correct this inadvertent typographical error.

In view of the foregoing comments and amendments, withdrawal of the rejection of Claims 45-87 under 35 U.S.C. § 112, second paragraph is respectfully requested.

Claims 45-60 and 64-75 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enabling support for treatment of disorders mediated by a growth factor other than IGF-I, or for treatment of skin capable of becoming inflamed or proliferating. In the interest of advancing prosecution, Claims 45 and 64 have been amended to delete the

phrase "or skin capable of proliferation," and Claims 47 and 48 have been cancelled without prejudice.

Claim 45 has been amended to clarify that the nucleic acids are capable of reducing the levels of IGF-I receptor. Support for this amendment may be found in the specification, for example at page 106, line 10 – page 109, line 9. Claim 64 is directed to a method of treating psoriasis with a specific nucleic acid, which, as the Examiner has acknowledged is enabled by the specification. Claim 76 has been amended to recite a composition comprising a specified nucleic acid, which compositions are enabled by the specification.

In view of the foregoing comments and amendments, withdrawal of the rejection of Claims 45-60 and 64-75 under 35 U.S.C. § 112, first paragraph is respectfully requested.

Claims 61-63, 76, 78 and 81 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated by WO 99/60855 to Wang. Applicants respectfully submit that WO 99/60855 was published after the priority date of the present application, and thus is not prior art under 35 U.S.C. § 102(a). Withdrawal of the rejection is respectfully requested.

Claim 61-63, 76, 78 and 81 have been rejected under 35 U.S.C. § 102(a) as allegedly anticipated by U.S. Patent No. 5,681,940 to Wang et al. The Examiner has alleged that Wang et al. disclose nucleic acids consisting of SEQ ID NO: 10 and SEQ ID NO: 14 and chemical analogues thereof. In the interest of advancing prosecution, Claims 61-63, 78 and 81 have been cancelled without prejudice, and Claim 76 has been amended. Withdrawal of the rejection is respectfully requested.

Claims 61-63, 76 and 79 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,643,788 to Baserga, or WO 96/10401 to Delafontaine or WO 98/22579 to Low et al., or under 35 U.S.C. § 102(e) in view of U.S. Patent No. 6,071,891 to Low et al. The Examiner has alleged that the cited references disclose 18-mer and 20-mer nucleic acid analogues of SEQ ID NO: 12. Claims 61-63 have been cancelled without prejudice. The 18-mers and 20-mers of the prior art are not chemical analogues of the nucleic acid of SEQ ID NO: 1, since chemical analogues as defined herein include nucleic acids in which a base, nucleotide, nucleoside or phosphate backbone is modified, but the number of bases is not changed. Accordingly, withdrawal of the rejections under 35 U.S.C. §§ 102(b) and 102(e) is respectfully requested.

Claims 45-51, 54, 61-66, 69, 76, 78 and 81 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 96/01636 to Werther et al. The Examiner has alleged that Werther et al. disclose methods of treatment of skin disorders using an 18-mer DNA analogue of SEQ ID NO: 14. As discussed above, the claims include the nucleic acid of SEQ ID NO: 14, and chemical analogues thereof, but chemical analogues as defined herein do not include the 18-mer nucleic acid of Werther et al. Withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

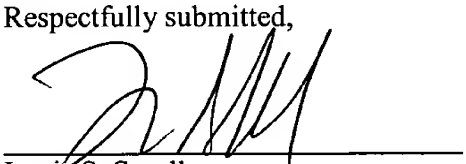
Claims 61-63 have been rejected under 35 U.S.C. § 102(b) as alleged anticipated by CN1231582A to Hu et al. In the interest of advancing prosecution, Claims 61-63 have been cancelled without prejudice.

Claims 45-50, 52, 64, 65 and 67 have been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by U.S. Patent No. 5,929,040 to Werther et al. in view of U.S. Patent No. 6,071,891 to Low et al., WO 98/22579 to Low et al., WO 96/10401 to Delafontaine or U.S Patent No. 5,643,788 to Baserga. The Examiner has alleged that Werther et al. teach methods of treatment of skin disorders using antisense molecules that inhibit IGF-I, and that the secondary references teach chemical analogues of SEQ ID NO: 12 that are antisense inhibitors of IGF-I. Applicants respectfully submit that none of Werther et al. nor the secondary references teach the nucleic acid of SEQ ID NO: 12 or a chemical analogue thereof as the latter is defined in accordance with the present invention. Thus, the combination of cited references fails to achieve the present invention. Withdrawal of the rejection under 35 U.S.C. § 103(a) is thus respectfully requested.

In view of the foregoing comments and amendments, favorable consideration and allowance of all pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please cancel Claims 47, 48, 61-63, 78 and 81 without prejudice.

Please amend Claims 45, 64, 76, 84 and 87 as follows.

45. (Amended) A method for ameliorating the effects of a proliferative and/or inflammatory skin disorder in a mammal, said method comprising contacting the proliferating and/or inflamed skin [or skin capable of proliferation and/or inflammation] with an effective amount of a nucleic acid molecule selected from the group consisting of 5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10); 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12); 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13); 5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14); 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15); 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16); 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17); 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18); 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19); 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or chemical analogue of any one of said nucleic acid molecules wherein said nucleic acid molecule or its chemical analogue is capable of [inhibiting or otherwise reducing growth factor mediated cell proliferation and/or inflammation and/or other medical disorders] reducing the level of IGF-I receptor in said mammal.

64. (Amended) A method of ameliorating the effects of psoriasis in a mammal, said method comprising contacting proliferating skin [or skin capable of proliferation] with an effective amount of one or more nucleic acid molecules or chemical analogues thereof [capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation wherein said one or more molecules comprises a polynucleotide] selected from the group consisting of 5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10); 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12); 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13); 5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14); 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15); 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16); 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17); 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18); 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19); 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or chemical analogue of any one of said nucleic acid molecules which is capable of interacting with mRNA [directed] transcribed from an IGF-I gene, an IGF-I receptor gene or a gene encoding an IGFBP.

76. (Amended) A composition [comprising a nucleic acid molecule capable of inhibiting or otherwise reducing IGF-I mediated cell proliferation, said composition] comprising a nucleic acid molecule selected from the group consisting of [5'-ATCTCTCCGCTTCCTTTC-3' (SEQ ID NO:10);] 5'-UCCGGAGCCAGACUU-3' (SEQ ID NO:12); 5'-CACAGUUGCUGCAAG-3' (SEQ ID NO:13); [5'-UCUCCGCUUCCUUUC-3' (SEQ ID NO:14);] 5'-AGCCCCCACAGCGAG-3' (SEQ ID NO:15); 5'-GCCUUGGAGAUGAGC-3' (SEQ ID NO:16); 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17); 5'-GGAUCAGGGACCAGU-3'

(SEQ ID NO:18); 5'-CGGCAAGCUACACAG-5' (SEQ ID NO:19); 5'-GGCAGGCAGGCACAC-3' (SEQ ID NO:20) or chemical analogue of any one of said nucleic acid molecules, wherein said nucleic acid or chemical analogue is capable of reducing the level of IGF-I receptor in a mammal said composition further comprising one or more pharmaceutically acceptable carriers and/or diluents.

84. (Amended) A composition according to Claim 76 wherein the nucleic acid molecule is 5'-UAACAGAGGUCAGCA-3' (SEQ ID NO:17) or chemical analogue thereof. [A method according to Claim 73 or 74 wherein the nucleic acid molecule is 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18) or chemical analogue thereof.]

87. (New) A composition according to Claim 76 wherein the [nucleicacid] nucleic acid molecule is [5'- GGCAGGCAGGCACAC-3' (SEQ ID NO:20)] 5'-GGAUCAGGGACCAGU-3' (SEQ ID NO:18) or chemical analogue thereof.